



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/598,518

02/06/2007

Philip Wilson Howard

065435-9080-US00

6779

23510 7590 03/13/2009
MICHAEL BEST & FRIEDRICH LLP
ONE SOUTH PINCKNEY STREET
P O BOX 1806
MADISON, WI 53701

EXAMINER

KIFLE, BRUCK

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

03/13/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/598,518	Applicant(s) HOWARD ET AL.	
	Examiner Bruck Kifle	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19, 21 and 23-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19, 21 and 23-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/06, 01/07, 08/08, 03/09</u> | 6) <input type="checkbox"/> Other: _____ |

Claim Rejections - 35 USC § 112

Claims 1-19, 21 and 23-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) In claim 1, the phrase “and salts and solvates thereof” should be rewritten as, for example, “or a pharmaceutically acceptable salt thereof” to comply with proper Markush language and limit the salt to a pharmaceutically acceptable salt as this appears to be the intended use of these compounds. See below for “solvates.”

ii) The groups R¹⁰ and R¹¹ are defined as “a carbamate-based nitrogen protecting group” and “an oxygen protecting group,” respectively. It is unclear from what these groups are supposed to be protecting. The compounds are final products and do not need protection from anything anymore. A clarification is required.

iii) The phrase “optionally substituted” without saying which substituents are intended is indefinite. One skilled in the art cannot say which substituents are permitted and which ones are not.

iv) The groups C₃₋₂₀ heterocyclyl and C₅₋₂₀ aryl are indefinite because it is not known how many heteroatoms are present, what kinds of heteroatoms are involved, what size ring is intended and how many rings are present. A heterocyclyl necessarily requires the presence of a hetero atom and cannot be made up of only carbon atoms. The lowest number of carbon atoms permitted in an aryl is 6. It is unclear what is intended by a C₅ aryl.

Art Unit: 1624

v) Claims 24 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the reaction steps from starting material to final product.

Claims 1-19, 21 and 23-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical salt, does not reasonably provide enablement for solvates of the compound of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Applicants have not shown how one skilled in the art can arrive at a given solvate. None of the compounds made are crystallized out as solvates. Arriving at a given solvate is not routine experimentation because it is unpredictable. One cannot make any solvate of a compound.

Solvates are different chemical entities, they are not just impurities included in a compound. Pharmaceutically acceptable salts are additions and therefore not the same. Additions are obvious variation “after” the compounds are obtained, thus, can be allowed with the compounds. Solvates or hydrates must be obtained at the time the invention was made. If Applicants do not have the solvates or hydrates at the time the invention was made, they are not in possession of them because they are unpredictable.

Claim 23 is drawn to the treatment of a proliferative disease. The specification does not provide enablement for the treatment of a proliferative disease generally. No compound has ever been found that can treat proliferative diseases generally even though massive efforts have been

Art Unit: 1624

directed towards this end. Since this assertion is contrary to what is known in oncology, proof must be provided that this revolutionary assertion has merits. Nearly all anticancer drugs are effective against only a limited group of related cancers. Therefore, a compound effective against a proliferative disease generally would be a revolutionary exception. Applicant is asserting that he succeeded where others have failed. Where extensive efforts have all failed, it is reasonable for the Patent and Trademark Office to require proof that the claimed invention actually works for this specific utility. It is well established that a utility rejection is proper when scope of enablement is not reasonably correlated to the scope of the claims. (In re Vaeck 20 USPQ2d 1439, 1444, In re Ferens 163 USPQ 609).

In re Buting 163 USPQ 689 establishes that even clinical tests showing that a compound found to be useful in the treatment of two types of cancers was not sufficient for a much broader range.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

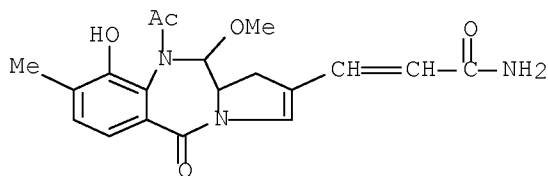
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ueda et al. (US 4,309,437). The claim reads on the compounds depicted below.

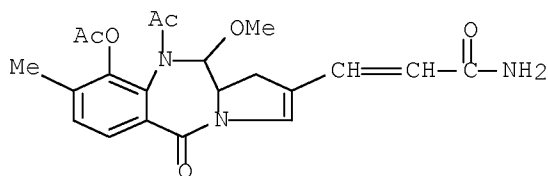
RN 77004-92-3 CAPLUS
CN 2-Propenamide, 3-(10-acetyl-5,10,11,11a-tetrahydro-9-hydroxy-11-methoxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (CA INDEX NAME)

Art Unit: 1624



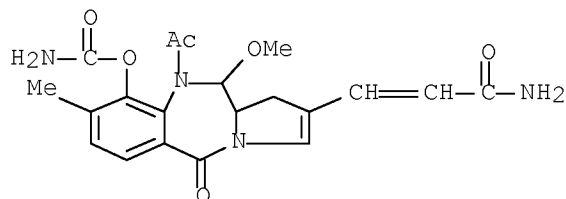
RN 77004-94-5 CAPLUS

CN 2-Propenamide, 3-[10-acetyl-9-(acetyloxy)-5,10,11,11a-tetrahydro-11-methoxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]- (CA INDEX NAME)



RN 77004-97-8 CAPLUS

CN 2-Propenamide, 3-[10-acetyl-9-[(aminocarbonyl)oxy]-5,10,11,11a-tetrahydro-11-methoxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]- (CA INDEX NAME)

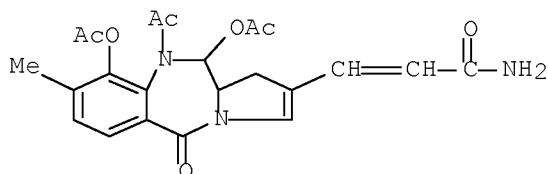


Claims 1, 11 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by

Leimgruber et al. (US 3,523,941). The claims read on the compounds depicted below.

RN 29455-46-7 CAPLUS

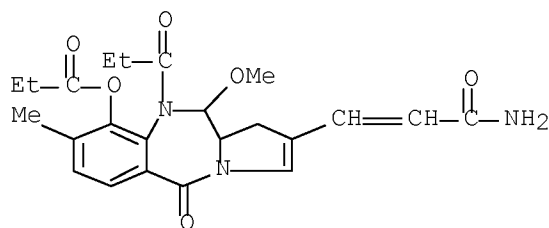
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 10-acetyl-5,10,11,11a-tetrahydro-9,11-dihydroxy-8-methyl-5-oxo-, diacetate (ester), (E)-(S,S)-(+)- (8CI) (CA INDEX NAME)



RN 29455-48-9 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 5,10,11,11a-tetrahydro-9-hydroxy-11-methoxy-8-methyl-5-oxo-10-propionyl-, propionate (ester), (E)-(11R,11aS)- (8CI) (CA INDEX NAME)

Art Unit: 1624



Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle whose telephone number is 571-272-0668. The examiner can normally be reached on Mondays-Fridays from 8:30 AM -6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruck Kifle/
Primary Examiner
Art Unit 1624

BK
March 11, 2009